ABOUT A CASE OF IDIOPATHIC DRAWFISM

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Objectives:
To report a case about Taybi linder syndrome which is very rare cause of dwarfism.
Taybi linder syndrome or microcephalic osteodysplastic primordial dwarfism type 1 (MOPD1) is characterized by an intrauterine and postnatal growth retardation, multiple malformations especially brain abnormalities.
The prognosis is poor with most of the reported patients dying within the first year of life.

Methods:
We report a case of a boy, 2 years and 3 months with a neonatal history of intrauterine retardation (birth weight 1700g) consults for stunting. At birth, constataion of a microcephaly, many investigations were made but no diagnosis was established.
At the clinical examination we found a dwarfism (−6,1 DS) (figure 4), microcephaly (occipital frontal circumference -7 DS)
Receding forehead, sparse hair and eyebrows, short neck (figure1), protruding eyes, small and low-set ears (figure 2), postaxial polydactyly and bilateral cryptorchidism (figure 3).
Dry skin and genu varum; Delay of psychomotor acquisitions
MRI: partial agenesis of corpus callosum, lissencephaly, diffuse parenchyme atrophy
Radiographics: bone dysplasia: short necf of femur, enlarged metaphyses, absence of epiphyses (figure 5).

Results:
• On the basis of clinical and radiological phenotype, the diagnosis made is microcephalic osteodysplastic primordial dwarfism type 1 for which there is no treatment.
• A genetic study would be done at the genetic departments of Necker hospital but unfortunately the patient died at the age of 2 years and 8 months.
• Microcephalic osteodysplastic primordial dwarfism (MOPD) type 1 (OMIM 210710) was recognized 45 years ago by the description of two siblings with dwarfism, skeletal abnormalities and brain malformations by Taybi Linder (1967). The syndrome was further delineated by Majewski and al (1982) as MOPD type I. Further major characteristics are extreme prenatal and postnatal growth retardation, severe microcephaly, unusual face and early death. The prevalence is unknown but less than 30 cases have been described in the literature.
• Mutations in the RNU4ATAC gene cause microcephalic osteodysplastic primordial dwarfism type I. It encodes U4atac, a small nuclear RNA that is a component of the minor spliceosome. Six distinct mutations in 30 patients diagnosed as microcephalic osteodysplastic primordial dwarfism type I have been described.
• The exact mechanisms by which decreased levels of spliceosomal complex RNAs might lead to the MOPD I phenotype remain unclear. Clues may be found by looking at other diseases caused by defects of the minor spliceosome. Although MOPD I is the first disease known to be associated with a defect in small nuclear RNA, it joins two other disorders defects in spliceosomal function – autosomal dominant retinitis pigmentosa and spinal muscular atrophy (SMA).
Treatment is supportive, prognosis is poor with most of the reported patients dying within the first year of life.

Conclusions:
Taybi linder syndrome or microcephalic osteodysplastic primordial dwarfism type 1 (MOPD1) the causative gene remains unknown but a mutation U4atac snRNA component of the minor spliceosome in the developmental disorder. Pronosis is fatal with death in the first or second year like our patient.

References:
1. De MOiC 2014-2015
2. ORPHANET
3. Microcephalic Osteodysplastic Primordial Dwarfism type 1 with biallelic mutations in the RNU4ATAC gene: Rebecca Nagy1,1, Hong Wang1, Beatrice Albrecht1, Dagmar Wiczkowski1, Gabrielle Gilles2, Karina Schlegel1, Eric Hartfi1, Peter Meinecke1, Albert de la Chapelle1,2, and Judith A. Westman1 Clin Genet. 2012 August ; 82(2)
4. Further delineation of the clinical spectrum in RNU4ATAC-related microcephalic osteodysplastic primordial dwarfism type 1 Ghada M.H. Abdel-Salam1,*, Mohamed G. Abdel-Hamid2, Mohamed S. Abdel-Hamid2, Mohamed A. Shouar2, Mohamed S. Isaa1, Laila Effat2, Mona S. Aglan1, and Maha S. Zaki3 American Journal of Medical Genetics Part A 2013

Figure 1
Figure 2
Figure 3
Figure 4
Figure 5